REMARKS/ARGUMENTS

By the present amendment, claims 18, 22-23, 26, 28 and 29 have been amended rendering claims 18, 20, 22-35 pending in the application. Claims 18, 22-23, 26, 28 and 29 have been amended as described below. The amendments to the claims have been made without prejudice and without acquiescing to any of the Examiner's objections. The amendment does not contain any new matter is its entry is respectfully requested.

The Office Action dated March 25, 2004 has been carefully considered. It is believed that the claim amendment and the following comments represent a complete response to the Examiner's rejections and place the present application in condition for allowance. Reconsideration is respectfully requested.

Objection to the specification

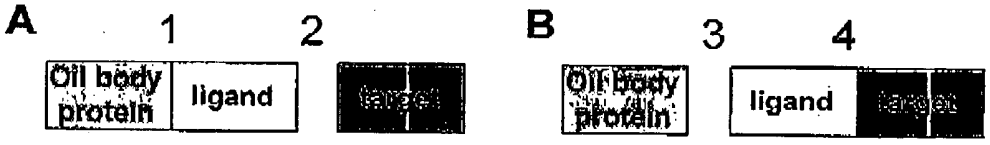
The Examiner has objected to the term "target molecule" as being ambiguous. In particular it is unclear as to whether or not the target molecule does or does not encompass oil body proteins (i.e., proteins naturally bound to oil bodies) including for example, oleosins. We respectively disagree for the following reasons.

The Examiner is correct that the specification defines the "target molecule" as the molecule that one wants to purify, which can be a recombinantly produced target molecule or one obtained from natural sources. The target also includes molecules that can directly associate with an oil body or oil body protein. Therefore, the definition in the specification is clear and no further clarification is required. However, for greater clarity, claims 18, 22, 26 and 29 have been amended to specify that the claimed target molecule is not an oil body protein, such as oleosin.

35 U.S.C. § 112

The Examiner has objected to claims 18, 20 and 22-35 under 35 U.S.C. §112 as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. We respectively disagree for the following reasons.

The Examiner specifically has indicated that "associates with the oil bodies" is unclear as to whether or not "associates with" refers to that which interacts with oil bodies via a direct *(covalently or non-covalently)* or via indirect means. The specification (page 10, line 34 to page 11, line 11) defines "associating with" as "including both covalent and non-covalent binding of the ligand to the oilbodies or the target molecule". For example, the ligand molecule may be covalently attached to the oil bodies (or oil body protein) and non-covalently associate with the target (and vice-versa), or the ligand may non-covalently associate with both the oil bodies and the target molecule." We respectively submit that the term "associates with the oil bodies" as used in claims 18, 22 and 29 refers to the covalent or non-covalent binding of the target molecule to the ligand, which in turn may be non-covalently or covalently bound to the oil bodies. As further described in the specification, page 11, lines 22-30, the ligand can be covalently attached to the target molecule by chemical or recombinant means (i.e. the ligand may be an antibody that is prepared as a recombinant fusion protein with the target) or the ligand may also be associated with a second molecule that can bind the target molecule (i.e. the ligand molecule may be an antibody conjugated to avidin and can be used to purify biotin from a sample). For further clarity we include the diagram below. In example A, the oil body protein and ligand are covalently bound (1) and the ligand is non-covalently bound to the target (2). In example B, the oil body protein and ligand are non-covalently bound (3) and the ligand and target are covalently bound (4).



The Examiner has also indicated that claims 18 and 29 are unclear in "the target molecule" because the claim does not make it clear as to whether or not said target molecule refers to a recombinant polypeptide to be isolated or an oil body protein. In response, claim 18 has been amended without prejudice in order to delete the phase "the target molecule" which clarifies that the target is the recombinant polypeptide. We respectively submit that in claim 29 that the phrase "the target molecule" is clear and refers to the molecule to be isolated and not an oil body protein.

The Examiner has indicated that claim 18 appears to be missing a step which refers to how the oil bodies are accessible to target molecule or/and the recombinant polypeptide in order to allow the oil bodies to contact with the target molecule and a ligand protein (claim 18, item 1). Furthermore, as claim 18 is directed to a method of isolating a recombinant polypeptide from a cell; thus, the claim must clarify how to contact the oil bodies with the ligand and the recombinant polypeptide.

We respectively disagree with the Examiner for the following reasons. As seen in the specification (page 28, lines 16 – page 29, line 14) the phrase "contacting the oil bodies with the recombinant polypeptide" means that the oil bodies are brought into proximity of the recombinant polypeptide in a manner that allows the recombinant polypeptide to associate with the oil bodies. In one embodiment, contacting of the recombinant polypeptide and the oil body is accomplished following the application of a technique resulting in the substantial disruption of the cell's integrity. In another embodiment, the contacting of the recombinant polypeptide and oil bodies is accomplished within the cell by expressing the recombinant polypeptide in a manner that allows the recombinant polypeptide to be directed intracellularly to the oil bodies. Having read the specification, a person of ordinary skill in the art would understand the phrase "contacting the oil bodies with the recombinant polypeptide".

In view of the above, we respectfully request that all of the objections to the claims under 35 U.S.C. §112 be withdrawn.

35 U.S.C. § 102

The Examiner has objected to claims 18, 22-23 and 26-29 under 35 U.S.C. § 102(b) as being anticipated by Moloney, M. (WO 96/21029). We respectively disagree for the following reasons.

The Examiner states that "Moloney teaches a method of isolating a polypeptide (a recombinant polypeptide) comprising contacting oil bodies with a protein ligand (i.e., oleosin) that associates with the oil bodies and said polypeptide, and isolating said oil bodies associated with said polypeptide that is to be isolated." Therefore, as noted by the Examiner, Moloney (WO 96/21029) teaches a situation where the protein ligand is an oleosin. However, we point out that independent claims 18, 22 and 26 all exclude the possibility of the ligand molecule being an oleosin. In particular, all of these claims specify that the ligand molecule "is not a protein that is normally associated with oil bodies".

We do not understand the Examiner's comment that because in WO 96/21029 "the oleosin protein is not a naturally occurring but rather recombinantly generated in a fusion protein", it is within the scope of the claim. We respectfully disagree as the specification clearly defines what is meant by "a protein that is normally associated with the oil body" on page 27, line 34 through to page 28, line 4. In particular, the definition states that such a protein includes proteins that normally associate with oil bodies in non-transformed normal cells, such as oil body proteins including oleosins. The fact that the oleosin is prepared as a recombinant fusion partner in WO 96/21029 does not exclude it from the definition. Therefore, the claims are clear in specifying that the ligand molecule does not include oloesin and therefore WO 96/21029 cannot be said to anticipate the claims.

The Examiner has objected to claims 18, 20, 22-28, 29-30, 32 and 34-35 under 35 U.S.C. § 102(b) as being anticipated by Moloney, M. (WO 93/21320). We respectively disagree for the following reasons.

The Examiner specifically refers to page 21, second paragraph of WO 93/21320, which describes the possibility of purifying the enzyme-oil body protein fusion protein using an antibody against the oil body protein. The Examiner states that this disclosure anticipates claims 18 and 20. We respectfully submit that WO 93/21320 does not anticipate claims 18 and 20 as these claims require a cell comprising the oil bodies and the recombinant polypeptide (the target molecule) that is contacted with a ligand molecule to associate the oil bodies and the recombinant polypeptide. The oil bodies associated with recombinant polypeptide are further isolated. In the passages described in WO 93/21320, the target molecule (enzyme-oil body protein fusion) is not present in a cell that comprises oil bodies when it is contacted with the antibody. In addition, for greater clarity, the independent claims 18, 22, 26 and 29 have been amended to specify that the claimed target molecule is not an oil body protein, such as oleosin.

The Examiner goes on to state that WO 93/21320 teaches the situation wherein the ligand is an oil body protein. As described above for WO 96/21029, the present claims do not include the possibility of the ligand being an oil body protein or oleosin, and therefore are not anticipated by WO 93/21320.

The Examiner has also indicated that WO 93/21320 involves disrupting the cell to allow association of the oil body with the recombinant protein and therefore anticipates claim 34 of the present invention. We respectfully disagree as in WO 93/21320, the recombinant protein is associated with the oil body through a direct fusion with an oil body protein and this association occurs during the formation of an oil body. In contrast, in claim 34 of the present invention, the recombinant protein is produced in the cell and association of the recombinant polypeptide occurs after substantial disruption of the cell's integrity (see specification, page 28, line 15 – page 29, line 7). Hence WO 93/21320 can not be said to anticipate claim 34 of the present invention.

The Examiner has also indicated that WO 93/21320 teaches a method of isolating a target protein from a host plant cell comprising (i) introducing into the cell a

polynucleotide encoding the said recombinant protein and a protein ligand (e.g. oil body protein) which results in fusion between the target and the oil body protein; (ii) growth the cell, and (iii) purifying said protein from the cell sample and therefore the teachings of WO 93/21320 meet the limitation of the application claim 22. In response to the Examiner's objections, claim 22 has been amended without prejudice to add the phrase "wherein said ligand molecule is not a protein that is normally associated with oil bodies".

Furthermore, the Examiner has objected to claim 25 as being anticipated by WO 93/21320 (Moloney), as Moloney teaches that in order to obtain the oil body fraction containing the oil body protein-recombinant polypeptide fusion, the plant cells are disrupted by lysis of the cells. We respectively submit that while the plant cells may be transformed with a polynucleotide encoding said fusion protein, the oil body protein-recombinant polypeptide fusion is formed during oil body biogenesis and not as a result of the lysis of the cells. Hence, WO 93/21320 can not said to anticipate claim 25.

The Examiner has also indicated that the Moloney's teaching (WO 93/21320) is applicable to claims 26 and 27 in that Moloney teaches a composition comprising oil bodies associated with a ligand (oleosin) that covalently linked (fused) to a target protein (an enzyme). In response to the Examiner's objection, claim 26 has been amended without prejudice to add the phrase "wherein said ligand molecule is not a protein that is normally associated with oil bodies".

The Examiner has objected to claims 18, 20, 22-23, 25-29 and 32-35 under 35 U.S.C. § 102(a) or (e) as being anticipated by Moloney, M. (US patent 5,650,554). We respectively disagree for the following reasons.

The Examiner has indicated that 5,650,554 anticipates claim 18 in that 5,650,554 teaches a method for isolating a polypeptide comprising contacting oil bodies with a hirudin ligand fused to the oleosin target molecule which associates with the oil body

through the hirudin ligand. Therefore, the Examiner is stating that in 5,650,554, the ligand molecule is hirudin which does not fall within the scope of the claims which requires that the ligand molecule associates with both the target molecule (e.g. a recombinant polypeptide) and the oil bodies. Hirudin does not associate with the oil bodies. Hence 5,650,554 can not be said to anticipate claim 18.

We respectfully do not understand the Examiner's statement "While Moloney does not teach that the antibody was recombinantly produced, this is different in recombinantly produced and naturally occurring." There is no mention of an antibody in the embodiment described by the Examiner.

Furthermore, the Examiner has objected to claim 20 as the hirudin can be considered to be a receptor polypeptide, and the antibody acts as a ligand since it "associates" with the oil body and the oleosin target molecule. Again, we do not understand the reference to an antibody in this context.

The Examiner has objected to claims 22 and 23 as being anticipated by in 5,650,554, Examples 3, 4 and column 27, lines 47-55. The purpose of Example 3, as set out in 5,650,554 (column 23, lines 16-18), was to demonstrate expression of the oleosin promoter and to determine the amount of 5' regulatory region required for expression in transgenic plants. The purpose of Example 4, as set out in 5,650,554 (column 24, line 66 – column 25, line 1) was to prepare a transgenic plant which expresses, under the control of the oil body promoter, fusion proteins which associate with oil bodies. Finally, the purpose of Example 6 was to illustrate that the activity of the GUS enzyme was maintained while fused to the oleosin protein and that the enzyme is accessible to substrate while attached to the oil bodies (column 27, lines 57-61). In response to the Examiner's objections, claim 22 has been amended without prejudice to add the phrase "wherein said ligand molecule is not a protein that is normally associated with oil bodies".

Furthermore, the Examiner has objected to claim 25 as being anticipated by 5,650,554 (Moloney), as Moloney teaches that in order to obtain the oil body fraction containing the oleosin-GUS fusion protein, the seeds are disrupted, i.e. ground in an extraction buffer. Claim 25 depends from claim 20, which depends on claim 18, which specifies that the protein ligand molecule is not a protein that normally associates with oil bodies. As a result, claim 25 is not anticipated by 5,650,554, as the ligand molecule cannot be an oleosin.

The Examiner has objected to claims 26-28 as being anticipated by 5,650,554 (Moloney) as the oil body fraction is a composition comprising the oil body associated with GUS ligand that is covalently attached to the target molecule, (i.e. oleosin protein). Claims 26-28 do not include within their scope an oleosin protein covalently attached to a target.

The Examiner has also objected to claims 29 and 35 as being anticipated by 5,650,554 (Moloney). Moloney teaches a method for separating a target molecule (oleosin) from a sample by contacting oil body with a protein ligand (GUS) and a target molecule (oleosin), and separating the oilbody and the target molecule from the sample (the oil body fraction comprising the target molecule oleosin protein). Hence, the Examiner is construing the ligand molecule to be GUS, which does not fall within the scope of the claims which require that the ligand molecule can associate with the oil bodies.

Furthermore, the Examiner has objected to claim 32 as 5,650,554 (Moloney) teaches that the sample is a seed, which meets the limitations "the sample is a cell" set forth in the application claim 32. Claim 32 depends on claim 29, which specifies that the protein ligand cannot be an oleosin. Accordingly, claim 32 cannot be anticipated by 5,650,554.

The Examiner has also objected to claim 33 as being anticipated by 5,650,554 (Moloney) as Moloney teaches that the target molecule oleosin is a protein, and GUS and oleosin were produced as a fusion polypeptide. Claim 33 depends from claim 29, which specifies that the ligand molecule cannot be an oleosin.

Finally, the Examiner has objected to claim 35 as being anticipated by 5,650,554 (Moloney) as Moloney teaches disrupting cell integrity by grounding transgenic *Brassica napus* seeds. Claim 35 depends from claim 29, which specifies that the ligand molecule cannot be an oleosin. Accordingly, claim 35 cannot be anticipated by 5,650,554.

In view of the forgoing, we respectively request that the objections to the claims under 35 U.S.C. § 102 be withdrawn.

Provisional Rejection – Obviousness Type Double Patenting

The Examiner has objected to claims 18, 20, 29-30 and 34-35 of this application as conflicting with claims 15, 9-10 and 15-16 of Application No. 10/260,562.

Applicant submits that a Terminal Disclaimer will be filed once it receives an indication that the present claims are in condition for allowance.

35 U.S.C. § 103

The Examiner has objected to claims 22-24 and 29-31 under 35 U.S.C. § 103 as being unpatentable over Moloney, M. (US 5,650,554). We respectively disagree for the following reasons.

The Examiner specifically states that it "would have been obvious to one of ordinary skill in the art at the time the invention was made to separate target molecule, e.g., oleosin by contacting oil bodies with antibody (including single chain antibodies) wherein the antibody acts as a ligand because Moloney suggests oil bodies associate with oleosin/antibody fusion protein have therapeutic or diagnostic value". As mentioned previously, the claims have been amended to clarify that neither the ligand nor the target molecule can be an oil body protein. Further, US Patent No. 5,650,554 is concerned with using oil body proteins to target the production of recombinant proteins to the oil bodies. However, US Patent No. 5,650,554 provides no motivation or suggestion to use

the oil bodies as tools for the purification of recombinant proteins as is claimed in the present application.

In view of the forgoing, we respectively request that the objections to the claims under 35 U.S.C. § 103 be withdrawn.

In view of the forgoing comments and amendments, we respectfully submit that the application is in order for allowance and early indication of that effect is respectfully requested. Should the Examiner deem it beneficial to discuss the application in greater detail, he is kindly requested to contact the undersigned by telephone at (416) 957-1682 at his convenience.

Respectfully submitted,

Maurice Moloney, Joseph Boothe and Gijs van Rooijen

Micheline Gravelle
Registration No. 40,261

MG/jl